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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/024,955	12/19/2001	Wayne Robert Thomas	IMI-032CP2DV	8377

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EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/024,955	THOMAS ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *80-92* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *81 and 87-89* is/are allowed.

6)☒ Claim(s) *80, 82-86, 90-92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment and response filed 5-15-04 have been entered into the record. Claims 1-79 have been cancelled. Claims 80-92 are pending and under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Withdrawn

Pursuant to the amendment of page 33 of the specification, the sequence requirements have now been met.

The amendment of the priority data is acknowledged.

Objections/Rejections Maintained

The objection to the specification as failing to provide proper antecedent basis for the claimed subject matter. Applicants have not traversed this objection and it is maintained for the record.

Claims 82-85 and 90-92 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reasons made of record for claims 82-85 and 90-92 in the Office action Mailed 1-12-04.

Applicants' arguments have been carefully considered but are not persuasive. Applicants argue that cross reactive proteins are defined in the specification at page 8, lines 5-8. Applicants argue that the specification teaches screening protocols to detect allergens that are cross-reactive (page 14, lines 13-22). This is not persuasive, the conception use of cross-reactivity to isolate polypeptides and polynucleotides that are cross -reactive does not provide conception by way of written description support for the converse. The concept of non-cross reactive epitopes is not presented in any of the

passages provided by Applicant. While the cited passages conveys that applicants had conceived that there would be cross-reacting family members of *Der p* VII *or Der f* VII, it does not convey cross-reactivity between *Der p* VII *and Der f* VII as alleged by applicants. Applicants' also argue that the specification at page 8, lines 5-8 provide for hybridizing nucleic acids from other animal species for use in screening assays to detect *Der p* VII *or Der f* VII or allergens, that are cross-reactive with *Der p* VII *or Der f* VII. Again, the use of cross-hybridizing nucleic acids in screening assays to detect allergens that are cross-reactive with *Der p* VII *or Der f* VII does not support conception of non-cross reactive epitopes as instantly claimed. Applicants argue that in order to determine the non-cross reactive epitopes, the peptides can be selected on the basis of various factors including the potential cross-reactivity of the peptide with other dust mite allergens (page 14, lines 13-22). The passage at page 14, lines 13-22 does not address cross-reactivity or non-cross reactivity. Applicants' thus appears to argue an enablement issue here, however the rejection of record is new matter which is conception by way of the non-cross reactivity as instantly claimed.

Support for the possible presence of cross-reactivity can not and does not provide for written description of conception of the converse. The specification clearly does not support that applicants had conceived at the time the invention was made, epitopes which were non-cross reactive as is instantly claimed. This rejection is applied to amended claim 86, because it recites the protein allergen is capable of inducing T cell proliferation "specific" (i.e. not cross-reactive) for Der f VII.

The rejection is maintained.

Claim 86 stands rejected under 35 USC 102(a) as being anticipated by Shen et al (Clinical and Experimental Allergy, 23:934-940, 1993; Reference CA on a filed PTOL-1449) is maintained for reasons previously made of record.

The claims recite that the isolated nucleic acid encoding a Der F VII protein allergen comprising an amino acid sequence that is at least 95% homologs to the amino acid sequence shown in SEQ ID NO:7 wherein the protein allergen is capable of inducing T cell proliferation specific for Der f VII (no structure recited). It is noted that any protein is capable of inducing a T cell response specific for itself. Further, the art defines homology as "similarity" and not "identity". There is no specific definition of homology as opposed to identity in the specification. Therefore, "homology" is given its art defined interpretation. As such, Shen et al anticipates the claimed invention because it is at least 95% "similar". Further, because Shen et al teaches regions of 100% identity it would generate a specific T cell response to itself and to Der f VII, in the absence of factual evidence to the contrary.

New Rejections Based on Amendment

Claim 86 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding a Dermatophagoides farinae VII (Der f VII) protein antigen comprising the amino acid as set forth in SEQ ID NO:7 , does not reasonably provide enablement for 95% homologous variants thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims recite an isolated nucleic acid encoding a Der f VII protein allergen comprising an amino acid sequence that is at least 95% homologous to the amino acid sequence shown in SEQ ID NO:7, wherein the Der f VII protein allergen is capable of inducing T cell proliferation specific for Der f VII. The teachings of the specification are limited to a single Der F VII protein allergen having the sequence as set forth in SEQ ID NO:7 and the nucleic acid encoding such as set forth in SEQ ID NO:6. The specification is devoid of any description of variants of SEQ ID NO:7 that are Der f VII protein

allergens. The claims merely recite that the Der f VII protein allergen is capable of inducing T cell proliferation specific for Der f VII. The recitation of Der f VII is not specifically limited and as such, the claim merely recites that any of the variants are capable of inducing T cell proliferation specific for itself. This is a circular limitation because any polypeptide is capable of inducing T cell proliferation specific for itself and is therefore not seen to be limiting to the scope of the variants claimed. The specification also teaches the homolog Der p VII. The specification does not teach what residues are varied to produce a Der f VII protein allergen as opposed to the Der p VII that is highly similar to Der f VII. The specification fails to teach the critical protein residues involved in the function of the protein SEQ ID NO:7 that define the genus of 95% equivalent Der f VII homologs as opposed to Der p VII homologs. One of skill in the art would be reduced to merely randomly altering amino acid(s) which would lead to unpredictable results regarding the functional activity of the protein as an protein allergen as claimed Protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid and sequences for different aspects of biological activity can not be predicted *a priori* and must be determined empirically on a case by case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3):1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be

an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. The specification has not conceived any other functionally equivalent protein sequences. The specification has not conceived any other DNA sequence variants of the family of Der f VII. The specification lacks a clear written description of a chemical structure of functional allelic variants or other proteins or polynucleotides having at least 95% homology, it is not enabled for this language because it fails to enable the skilled artisan to envision the detailed chemical structure of the claimed protein or DNA sequences coding for these proteins, as well as the method of obtaining it. In view of the lack of enabling written description of how to obtain, make and use the protein allergen homologs or DNA encoding the homologs that belong to the Der f VII family as opposed to the highly related Der p VII protein allergen one of skill in the art would be unable to produce either the proteins encompassed by the percent homology

In view of the lack of specific written description of conception of protein or DNA homologs, the lack of an enabling written description of how to obtain, make and use the protein homologs or the DNA encoding the protein homologs protein allergens having at least 95% sequence homology to a sequence of SEQ ID NO:7, the unpredictability associated with producing and using the myriad of homologs encompassed in the scope of the claims, the lack of to teach even a beginning point for variation of the protein sequence for routine experimentation, lack of working examples commensurate in scope with the instant claims, the skilled artisan would be forced into undue experimentation to practice (i.e. make and use) the invention as is broadly claimed.

Claims 80 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 80, the claim recites "...nucleotide bases 48-681 of the nucleotide sequences as set forth in SEQ ID NO:6." This language claim renders the metes and

bound of the language of the claim indefinite because SEQ ID NO:6 is a single nucleotide sequence and can not represent plural independent sequences. It is believed that the recited plurality is an inadvertent typographical error. Applicants should delete the "s" from "sequences" to resolve this issue.

Status of Claims

Claims 81 and 87-89 are allowable. Claims 80, 82-86 and 90-92 stand rejected.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-F 6:30 am - 3:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Pat a Duffy

Patricia A. Duffy

Primary Examiner

Art Unit 1645